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TITLE: Prostate Cancer Biorepository Network

PRINCIPAL INVESTIGATOR: Jonathan Melamed, MD

RECIPIENT: New York University
New York, NY 10016

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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4. TITLE AND SUBTITLE

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5b. GRANT NUMBER
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5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

New York University School of
Medicine
550 First Avenue
New York, NY 10016

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The goal of this proposal is to contribute as a network site to the continued development of infrastructure and operations of the Prostate Cancer Biorepository Network (PCBN). The aim of the PCBN is to provide prostate researchers with high-quality, well-annotated biospecimens obtained in a systematic, reproducible fashion using optimized and standardized protocols. The PCBN is funded as a consortium of participating network sites that includes New York University, under the overall guidance of the coordinating center at Johns Hopkins. The NYU network site works collaboratively to contribute to the PCBN goals, through infrastructure development, biospecimen accrual and biospecimen specialized processing and disbursement to investigators. The NYU network site procures specimens from more than 3 facilities, from primary localized as well as metastatic prostate cancer patients and stores them to maintain high quality biospecimens. Additionally clinical data including pathology and outcome data are annotated with the biospecimens. Specialized processing consists of tissue microarray design and construction. Biospecimens (mainly tissue microarrays) are disbursed to investigators approved through the PCBN. The combined efforts of the network site enables the PCBN consortium to successfully provide much sought after biospecimens for prostate cancer research.

15. SUBJECT TERMS

Prostate Cancer, Biorepository, tissue microarrays, tissue bank

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE		13	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION:

The goal of this proposal is to contribute to the continued development of infrastructure and operations of the Prostate Cancer Biorepository Network (PCBN). A prostate cancer biorepository fulfils an important need to enable prostate cancer research to be conducted by the wider research community due to the unavailability of biospecimens. Only few academic centers with high volume prostate cancer clinical services and an already developed banking infrastructure are well positioned to enable biospecimen collection. An external funding source as provided by the DOD enables support for a consortium of institutional biorepositories that can provide to the wider research community.

The major goal of the PCBN is to develop a biorepository with high-quality, well-annotated biospecimens obtained in a systematic, reproducible fashion using optimized and standardized protocols. The PCBN is funded as a consortium of participating network sites that include: New York University, Johns Hopkins, University of Washington and Memorial Sloan Kettering, under the overall guidance of the coordinating center at Johns Hopkins. The goal of the NYU network site is to collaboratively contribute toward the PCBN goals, through participation in infrastructure development, biospecimen accrual and derivative product development for the purpose of disbursement to investigators to enhance prostate cancer research.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Prostate cancer, biorepository, biomarkers, tissue microarrays, tissue bank

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

Task 1. *Review of sources of patients and biospecimens at site that can be made available to the repository (Month 1): Completed in 1st quarter (October 2014)*

Task 2. *Data elements used to annotate demographic, clinical, pathology, and biospecimen life cycle will be provided to the Coordinating Center, and the Network Site will participate in in the process of defining and harmonizing a set of common data elements (CDEs): Completed in 1st quarter (October 2014)*

Task 3. *Submit SOPs currently in use to Coordinating Center (Month 1): Completed in 1st quarter (October 2014)*

Task 4. *Participate in development of draft SOPs, common consent formats, and MTA (Months 1-6): Completed in 1st quarter*

Task 5. Report on performance metrics (Month 6): Ongoing (accrual reports provided on quarterly basis)

Task 6. Continue offering existing biospecimens to the research community (Months 6-36): Ongoing – we continue to offer biospecimens to the research community.

Task 7. Participate in SOP training (Month 9): New staff trained in SOPs in first and second quarter (100%)

Task 8. Annotate, perform quality control for processing, storage and clinical data collection, and distribute specimens (Months 10-36): Quality control steps for data collection performed (20%)

Task 9. Report on performance metrics (Months 12, 18, 24, 30, 36): Reported herein

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Major activities:
The major activities of the NYU network site are detailed under the following areas
Regulatory approval 2) Biospecimen accrual 3) Specimen characterization and data annotation 4) Specialized processing of biospecimens 5) Biospecimen disbursement

1) **Regulatory Approval: NYU**

Regulatory approval: The NYU site includes several hospital facilities, each of which requires its own approval for conduct of activities. NYU has access to three hospitals: NYU Langone Medical Center, Bellevue (an HHC hospital) and the New York Harbor VA hospital and all are actively involved in case recruitment. The NYU site maintains compliance with IRB issues in accordance with the NYU IRB, VA IRB and recommendations by the U.S. Army Medical Research and Materiel Command's (USAMRMC) Office of Research Protections (ORP), (Human Research Protection Office (HRPO).
The annual renewal for NYU Langone Medical Center and Bellevue Hospital Center was submitted to the NYU IRB on 03/09/2015 approved by NYU IRB on 3/23/2015. Bellevue Hospital Center provided approval on 07/06/2015. The NYU Langone Medical Center (A-18319 a) renewal was submitted to HRPO on 4/24/2015 (further inquiry on 10/16/2015).
The annual renewal for the NY Harbor VA was submitted to the VA IRB (Subcommittee for Human Studies, VA Medical Center, New York Harbor Healthcare System (NYHSS) Institutional Review Board (IRB) on 08/14/2015 with approval on 9/9/2014 for 1 year (expiration 9/8/2015). This was submitted to HRPO (A-18319 b) on 10/3/2014 and approved on 12/1/2014.
The most recent annual renewal for the NY Harbor VA was approved on 08/24/2015 for 1 year (expiration 08/23/2016)
The official tissue bank license from the NY State Department of Health (received in August 16th, 2013) was renewed on August 15, 2014 with expiration on September 1st 2016.
Both IRBs provide continued approval of a rapid autopsy program at each site. Additionally HRPO maintains oversight of these programs related to the Use of Human Cadavers for Research Development Test & Evaluation (RDT&E).

Regulatory Approval: Other potential collaborating sites

We have obtained IRB approval to add other sites as collaborating institutions for access to archival material:
Woodhull Hospital: approved by NYU IRB on 9/23/2014
The Brooklyn Hospital: approved by TBH IRB on 2/23/2015
SUNY Downstate: approved by SUNY IRB on 06/15/2015 and by NYU IRB on 11/20/2015
Although IRB approval has been provided for Woodhull Hospital, we await finance approval of the protocol and have been in discussion with administration at this facility related to proposed charges. A material transfer agreement between NYU and SUNY Downstate is pending approval.
Outreach for access to archival material at other collaborating sites: The NYU site has been reaching out for access to archival materials from other institutions which have a high volume of African American prostate cancer patients. These institutions include local public, state and private hospitals. Access to these sites requires a participating collaborator and regulatory approval (both IRB and legal). IRB Access to material from SUNY Downstate and the Brooklyn Hospital has been provided, however the process for legal access to Woodhull the public hospitals has been drawn out and painstakingly slow. We await further communication with the central HHC research leadership to determine whether access should be pursued.

2) **Accrual of Biospecimens (fresh frozen & formalin fixed paraffin embedded tissue and serum/plasma)**

The NYU site accrues fresh and frozen tissue and biofluids including serum, plasma and urine at all hospital sites.

The accrual according to hospital site is detailed in table1 below:

Table 1: Accrual of Biospecimens at NYU by Hospital site	NYU Total (mets/Aut)	BH Total (mets/Aut)	VA Total (mets/Aut)	Total (Metastatic patients/ rapid autopsy candidates)
Patients Consented	140 (0/0)	24 (8/1)	54 (43/8)	218 (51/9)
Surgery Performed	151	14	10	175
Frozen Tissue	145 (0/0)	10 (0/0)	10 (0/0)	165 (0/0)
Serum	74 (0/0)	16 (3/0)	82 (73/0)	172 (76/0)
Plasma	2 (0/0)	5 (1/0)	8 (3/0)	15 (4/0)
Buffy Coat	2 (0/0)	5 (1/0)	8 (3/0)	15 (4/0)
Urine	77 (0/0)	6 (0/0)	9 (0/0)	92 (0/0)
Prostatic Fluid	112 (0/0)	5 (0/0)	2 (0/0)	119 (0/0)
Seminal Vesicle Fluid	81 (0/)	4 (0/0)	1 (0/0)	86 (0/0)

The accrual per quarter is shown in tables 2a – d below:

Table 2a: Biospecimen Acquisition Oct 1- Dec 31 2014	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	42
Metastatic	15
Total	**57**
Tissue	
Radical Prostatectomy	68
Fluids	
Prostatic fluid	37
Seminal Vesicle fluid	35
Urine (Pre-Radical Prostatectomy)	46
Total	**243**

Table 2b: Biospecimen Acquisition Jan 1 – March 31 2015	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	32
Metastatic	11
Total	**43**
Tissue	
Radical Prostatectomy	36
Fluids	
Prostatic fluid	27
Seminal Vesicle fluid	20
Urine (Pre-Radical Prostatectomy)	20
Total	**146**

Table 2c: Biospecimen Acquisition April 1– June 30 2015	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	12
Metastatic	4
Total	**16**
Tissue	
Radical Prostatectomy	31

Fluids	
Prostatic fluid	12
Seminal Vesicle fluid	18
Urine (Pre-Radical Prostatectomy)	12
Total	**89**

Table 2d: Biospecimen Acquisition July 1– Sept 30 2015	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	24
Metastatic	2
Total	**26**
Tissue	
Radical Prostatectomy	30
Fluids	
Prostatic fluid	11
Seminal Vesicle fluid	9
Urine (Pre-Radical Prostatectomy)	14
Total	**90**

The biospecimen procurement is a streamlined process at all three hospitals; however accrual volume relies on several recruitment factors. These include adequate communication and alerts from Urology and Oncology colleagues of patients for recruitment and the need for consent to be provided by the patient to biorepository personnel. An important influence on accrual is of course volume of radical prostatectomy at each hospital. The highest volume is performed at NYU Langone medical center where the willingness of patients to consent is also high. In the public hospital (Bellevue) and the VA Hospital settings, surgical volume is lower and communication and surgery tracking modalities are less structured. An additional challenge at these 2 hospitals is the wariness of patients to participate in studies which results in a lower consent rate. The NYU access to metastatic cases is however primarily at these two hospitals and enabled by the participation and collaboration of the oncology staff including fellows and attending oncologists. We however have continued difficulty in getting most patients to agree to rapid autopsy. We have the cooperation of palliative care physicians who have assisted in communicating initially with patients. The candidacy of this patient population for rapid autopsy is made more challenging based on the limited resources and limited family contact of some of the patients.

3) Specimen Characterization and Data annotation:

The clinical data for the current archive of specimens is updated on a regular basis through access to the electronic medical record (EPIC, Quadramed and CPRS), Pathology database (Powerpath), Urology research databases and tumor registry records. As there is no electronic interface between the electronic record systems and the biorepository database, import of data requires either modifications of downloaded excel and PDF files or manual entries which are slow processes. The clinical data update is therefore performed on a regular ongoing basis, with quality control checks (relook at a subset of cases) to assure accuracy. Prospective cases are added on a daily basis, while update of biorepository records is done in groups at least twice per week. Additionally, tissue microarray data is updated on a regular basis (6 monthly for biochemical recurrence TMA). Pathology data is updated on a weekly basis with additional access to prostate cancer maps which allow characterization of focality (in preparation for multifocal TMA). Frozen section characterization is performed on the procured samples within days of the surgery and slides are annotated for tumor distribution and Gleason grade and both annotated into the Biorepository database as well as scanned to include images.
These data annotation processes require significant effort in “copy and paste”, therefore we are working with the informatics group at NYU (Under Michael Cantor) and an external informatics consulting group (Essex group) to introduce use of several natural language extraction tools and use of I2B2 tools to make this a more automated process.

4) Specialized Processing (Derivatives) of Accrued Biospecimens

Tissue Microarrays (TMAs): The NYU site continues to provide several TMA sets to PCBN that are regularly requested by investigators. Additionally other TMA sets are under design and construction. These include:
Biochemical Recurrence TMA: The current TMA that NYU has provided to PCBN is the 217 BCR TMA that enables assessment of biomarkers strongly associated with known prognostic factors (e.g. stage, grade). It includes patients with versus without biochemical recurrence, to a total of 217 cases, 23 with adjacent normal (4-5 tumor cores, 4 normal cores) and 13 BPH cases (4 cores). Since this TMA is frequently sought we have worked to construct at 600+ biochemical recurrence TMA and are close to release of this TMA once quality control checks (presence of tumor in cores and p27 antigenicity) have been performed.
Hormone Sensitivity TMA: The NYU site provides a 56 case Hormone sensitivity TMA, which enables testing of biomarkers associated with androgen biology. It includes hormone naive versus hormone refractory cases totaling 56 cases; 18 hormone resistant, 18 hormone naïve, 10 radical prostatectomy (RP) cases with neo adjuvant treatment, 10 RP without neo adjuvant treatment, 5 normal from RP with neo adjuvant treatment and 5 normal RP without neo adjuvant treatment. Due to the rarity of pathology samples after androgen therapy, this TMA required searching across the entire archive for possible cases. We have worked to identify more cases and are working to expand this TMA through providing a larger number of hormone resistant cases. The cases are identified and the TMA awaits construction.
Multifocality TMA: The NYU site is working to construct a TMA that allows comparison of biomarkers across separately identifiable tumor foci. Prostate maps have been drawn from slide reconstructions and blocks selected to allow construction of this TMA. Some of the design is still under consideration however we are currently collecting blocks for construction.
The instrument used for construction at NYU is a semi-automated Beecher TMA instrument (MTA-1). This was customized as a semi-automated instrument by an engineering student at University of Wisconsin through collaboration with colleagues at the institution. Due to a recent electrical disruption, the instrument is no longer motorized and unable to function. We therefore are using a manual TMA instrument (Beecher MTA-1) on loan from the department of Pathology for TMA construction. We are in discussion with the original engineer to provide an estimate for repair of this instrument.

5) Disbursement of Biospecimens

Tissue microarray sets were provided to investigators as follows:
217 case Biochemical recurrence TMA (1 set) to investigator at Georgetown University
217 case Biochemical recurrence TMA (1 set) to investigator at University of Illinois
114 Race Disparity TMA (3 sets) to investigator at Johns Hopkins University
Biochemical recurrence TMA (1 set) to an investigator at University of Pittsburgh.
High grade PIN TMA (1 set) to an investigator at Johns Hopkins University.

Disbursement of biospecimens is primarily of tissue microarray sets. In order to make these more useful to investigators we have prepared product datasheets which outline the design, layout, construction, quality assurance steps and control tissues of the tissue microarrays. These datasheets are available for the biochemical recurrence and hormone sensitivity TMAs.

What opportunities for training and professional development has the project provided?

Nothing to Report

How were the results disseminated to communities of interest?

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We plan to 1) continue accrual of biospecimens 2) to prepare tissue microarrays with associated data 3) to pilot a more streamlined an automated process for data annotation 4) to increase rapid autopsy recruitment and to 5) work to establish access to partnering organizations archival prostate cancer tissue

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?
.

Nothing to Report

What was the impact on society beyond science and technology?
.

Nothing to Report

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

A change in leadership of the NYU core tissue procurement service has resulted in the departure of the technical assistant who procured tissue from surgical specimens and who assisted with radical prostatectomy prosection. We have therefore trained other persons including pathology assistants and the uropathology fellow on the SOP for procurement. Currently procurement is provided by a group of persons until the institution core recruits a replacement pathology assistant (expected within 2 months).

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Delays were incurred due to inadequate staffing after the departure of resource personnel and delay in hiring of new personnel. Other delays are incurred due to faulty instrument (semi-automated tissue microarrayer) that can only be repaired by the initial engineer that customized IT. This is resolved by use of a substitute tissue microarrayer however this is more cumbersome to use. We intend to have the instrument repaired if possible by the original engineer, otherwise will use

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Biorepository personnel (biorepository manager and research coordinator) left the institution for other job opportunities. There was a delay in hiring of staff to replace them, which resulted in a decrease in expenditure.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

None reported

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**

  Journal publications.

  Nothing to Report

  Books or other non-periodical, one-time publications.

  Nothing to Report

  Other publications, conference papers, and presentations.

  Nothing to Report

- **Website(s) or other Internet site(s)**

  Nothing to Report

- **Technologies or techniques**

  Nothing to Report

- **Inventions, patent applications, and/or licenses**

  Nothing to Report

- **Other Products**

Research material: Biospecimen accrual – see table	
Type of biospecimen	Number
Frozen Tissue	165
Serum	172
Plasma	15
Buffy Coat	15
Urine	92
Prostatic Fluid	119

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: *Jonathan Melamed MD*
Project Role: *PI*
Researcher Identifier (ORCID ID): orcid.org/0000-0003-2844-7990
Nearest person month worked: *2*
Contribution to Project: *Dr. Melamed has oversight of project*

Name: *Peng Lee MD PhD*
Project Role: *Co-investigator*
Researcher Identifier (e.g. ORCID ID): 1234567
Nearest person month worked: *1*
Contribution to Project: *Dr. Lee oversees activities at the NY Harbor VA.*

Name: *Ruth Pe Benito MPH*
Project Role: *Research Scientist & Biorepository* manager
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *5*
Contribution to Project: *Ms. Pe Benito* manages and oversees the day-to-day functioning of the Cancer Biorepository assists with translational research studies
.

Name: *Allison Maresca BS*
Project Role: *Research coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *6*
Contribution to Project: *Ms. Maresca is* responsible for biofluid and tissue procurement, data extraction for the existing paraffin embedded cases in NYU archives and data entry of new cases into IRB compliant database..

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

Organization Name: Woodhull Hospital
Location of Organization: Brooklyn, New York
Partner's contribution to the project: Collaboration

Organization Name: The Brooklyn Hospital
Location of Organization: Brooklyn, New York
Partner's contribution to the project: Collaboration

Organization Name: SUNY Downstate Hospital
Location of Organization: Brooklyn, New York
Partner's contribution to the project: Collaboration

Organization Name: Brooklyn VA Hospital
Location of Organization: Brooklyn, New York
Partner's contribution to the project: Collaboration

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.